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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/042,583	03/17/98	NI J	PF366

022195
HUMAN GENOME SCIENCES INC
9410 KEY WEST AVENUE
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HM22/0526

EXAMINER	
KAUFMAN, C	
ART UNIT	**PAPER NUMBER**
1646	6

DATE MAILED: 05/26/99

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary	Application No.	Applicant(s)	
	09/042,583	NI, ET AL.	
	Examiner	Art Unit	
	Claire M. Kaufman	1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).

Status

1)☒ Responsive to communication(s) filed on *22 September 1998* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-34* is/are pending in the application.

4a) Of the above claim(s) *19-21 and 24-28* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-18,22,23 and 29-34* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claims *1-34* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

a)☐ All b)☐ Some * c)☐ None of the CERTIFIED copies of the priority documents have been:

1.☐ received.

2.☐ received in Application No. (Series Code / Serial Number) _____ .

3.☐ received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. & 119(e).

Attachment(s)

14) ☒ Notice of References Cited (PTO-892)
15) ☒ Notice of Draftsperson's Patent Drawing Review (PTO-948)
16) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *4* .
17) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
18) ☐ Notice of Informal Patent Application (PTO-152)
19) ☐ Other: .

DETAILED ACTION

1. The preliminary amendment filed Sept. 22, 1998 has been entered.

2. The Group and/or Art Unit location of your application in the PTO has changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Group Art Unit 1646.

Election/Restrictions

3. Restriction to one of the following inventions is required under 35 U.S.C. 121:

I. Claims 1-18, 22, 23 and 29-34, drawn to nucleic acid, vector and host cell, classified in class 435, subclass 69.1.

II. Claims 19-20, 24-25, 27 and 28, drawn to polypeptide and pharmaceutical composition, classified in class 530, subclass 350.

III. Claims 21 and 26, drawn to antibody and pharmaceutical composition, classified in class 530, subclass 388.22.

The inventions are distinct, each from the other because of the following reasons:

The nucleic acid of Invention I is related to the polypeptide of Invention II by virtue of encoding the same. The nucleic acid molecule has utility for the recombinant production of the polypeptide in a host cell, as recited in claim 34. Although the nucleic acid molecule and polypeptide are related since the nucleic acid encodes the specifically claimed polypeptide, they are distinct inventions because the polypeptide can be made by another and materially different process, such as by synthesis or purification from the natural source. Further, the nucleic acid may be used for processes other than the production of the polypeptide, such as nucleic acid hybridization assay for detection of related nucleic acids.

The nucleic acid of Invention I is related to the antibody of Invention III by virtue of the nucleic acid encoding the polypeptide of Invention II, which is the cognate antigen of the antibody and necessary for production of the antibody. However, both the nucleic acid and encoded polypeptide of Inventions I and II, respectively, are distinct from the antibody of

Invention III. The reasons for this is that although the polypeptide and antibody are related due to their necessary stearic complementarity, they are distinct inventions because the polypeptide can be used for another and materially different process other than for production of the antibody, such as in a pharmaceutical composition in its own right, or to assay or purify the natural ligand of the polypeptide (as the polypeptide is itself a receptor), or in assays for the identification of agonists or antagonists of the receptor polypeptide. Because the nucleic acid is structurally unrelated to the antibody and the polypeptide it encodes is distinct from the antibody, so is the nucleic acid.

Because these inventions are distinct for the reasons given above, have acquired a separate status in the art as shown by their different classification and because of their recognized divergent subject matter, and the search required for Invention I is not required for Invention II or III, and the search for Invention II is not required for Invention III, restriction for examination purposes as indicated is proper.

4. During a telephone conversation with A. Anders Brookes on December 10, 1998 a provisional election was made with traverse to prosecute the invention of Group I, claims 1-18, 22, 23 and 29-34. Affirmation of this election must be made by applicant in replying to this Office action. Claims 19-21 and 24-28 withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention.

Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a petition under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

Oath/Declaration

5. The oath or declaration is defective. A new oath or declaration in compliance with 37 CFR 1.67(a) identifying this application by application number and filing date is required. See MPEP §§ 602.01 and 602.02.

The oath or declaration is defective because:

The full name of each inventor (family name and at least one given name together with any initial) has not been set forth.

It does not identify the city and state or foreign country of residence of each inventor.

It does not identify the citizenship of each inventor.

It does not identify the post office address of each inventor. A post office address is an address at which an inventor customarily receives his or her mail and may be either a home or business address. The post office address should include the ZIP Code designation.

It appears that at least one full given name of applicant Ni, Gentz and Yu is not present either in the signature or elsewhere in the papers. This application will not be passed to issue until the omitted name has been supplied or unless a statement has been supplied over the applicant's signature setting forth that the name as signed is the actual full name of applicants above. See MPEP § 605.04.

It appears that the substitute declaration field May 11, 1998 is missing several pages. It appears that the first and last pages were received, but pages containing the above listed information including the signatures of Ni, Gentz and Yu are missing.

Drawings

6. Figure 1 of the instant application is presented on two separate panels. 37 C.F.R. § 1.84 (u)(1) states that when partial views of a drawing which are intended to form one complete view, whether contained on one or several sheets, must be identified by the same number followed by a capital letter. The two sheets of drawing which are labeled "Figure 1" in the instant specification should be renumbered "Figure 1A and 1B". Applicant is reminded that once the drawings are changed to meet the separate numbering requirement of 37 C.F.R. § 1.84 (u)(1), Applicant is required to change the Brief Description of the Drawings and the rest of the specification accordingly. If, for example, Figure 1 is divided into Figures 1A and 1B, then the Brief Description and all references to this figure in the specification must refer to Figures 1A and/or 1B.

Sequences Presented in Drawing Figures

7. 37 CFR 1.821(b) requires exclusive conformance, with regard to the manner in which the nucleotide and / or amino acid sequences are presented and described, with the sequence rules for all applications that include nucleotide and amino acid sequences that fall within the definitions. When a sequence is presented in a drawing, regardless of the format or the manner of presentation of that sequence in the drawing, the sequence must still be included in the Sequence Listing and the sequence identifier ("SEQ ID NO:X") must be used, either, in the drawing or in the Brief Description of the Drawings. (See MPEP 2422.02.) Figure 4 shows two sequences which the specification identifies on page 12, paragraph 2, as SEQ ID NO:6 and 7. Either the figure or the Brief Description must reference these SEQ ID NOs.

Claim Rejections - 35 USC § 112, First Paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

8. Claims 1, 8, 11-17, 23 and 29-33 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a polynucleotide that is at least 95% identical to a polynucleotide encoding a polypeptide with one of the amino acid sequences listed in (a)-(c) of the claim or to the cDNA clone in ATCC No. 97920 or to a nucleic acid encoding a polypeptide encoded by the cDNA clone in ATCC No. 97920 or a nucleic acid complementary thereto, does not reasonably provide enablement for a nucleic acid encoding a DR5 extracellular domain (ECD), transmembrane domain (TMD), intracellular domain (ICD), or death domain (DD) or complementary nucleic acid thereto or a nucleic acid 95% identical to the DR5 domain-encoding nucleic acid or polypeptide which is the same as a polypeptide consisting of one of the amino acid sequences listed in the claim, except for having at least one conservative amino acid

substitution. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The factors considered when determining if the disclosure satisfies the enablement requirement and whether any necessary experimentation is undue include, but are not limited to:1) nature of the invention, 2) state of the prior art, 3) relative skill of those in the art, 4) level of predictability in the art, 5) existence of working examples, 6) breadth of claims, 7) amount of direction or guidance by the inventor, and 8) quantity of experimentation needed to make or use the invention. In re Wands, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988).

The claims are drawn to nucleic acid molecules that are structurally related (either identical or 95% identical) to a specific nucleotide sequence or to a nucleotide sequence encoding a specific amino acid sequence. However, the claims are also drawn to nucleic acid molecules structurally related to particular domains of a DR5 polypeptide. While one could make and use a nucleic acid that is structurally related to a nucleic acid that has a particular sequence (e.g., SEQ ID NO:1 or the cDNA in ATCC No. 97920), the specification does not teach how to make or use a nucleic acid that encodes a DR5 domain with a sequence other than that comprised by SEQ ID NO:2. The DR5 polypeptide of SEQ ID NO:2 was shown to influence apoptosis (see Examples 5 and 6). There is no limiting definition in the specification of what a DR5 polypeptide is so that one of skill in the art would know what properties—either structural or functional--the encoded DR5 polypeptide or domain thereof must have. The specification says that a DR5 polypeptide can have the sequence of SEQ ID NO:2 (emphasis added by Examiner), but does not say what other DR5 polypeptide sequences can be. Also, the sequences of the particularly recited domains of the DR5 polypeptide of SEQ ID NO:2 are also disclosed (p. 11, lines 15-24). However, the DR5 domains recited in the claims are not identified by either sequence or function.

The prior art does not teach a DR5 polypeptide or encoding nucleic acid. Other DR-related polypeptides are taught, and they are involved in apoptosis (e.g., Chinnaiyan et al., Science, 1996, cited by Applicants). It is acknowledged that the skill in the art is high. There is

no disclosure of what properties ~~as~~ aside from the sequence of SEQ ID NO:2 make DR5 unique compared to other DR-related polypeptides. Therefore, the specification does not provide guidance for the skilled artisan to distinguishing a claimed DR5 polypeptide, which is not identified by sequence, from other DR-related polypeptides. There is only one example of a DR5 polypeptide and encoding nucleic acid, however, it is well within the skill of the artisan to make nucleic acids which are degenerate to the nucleic acid of SEQ ID NO:1 so that they still encode the polypeptide of SEQ ID NO:2. For these reasons, it would require undue experimentation to make the invention commensurate in scope with the great breadth of the claims.

Additionally, because claim 23 is drawn to a polynucleotide encoding a polypeptide that has the sequence of SEQ ID NO:2 or a specified portion thereof, except for at least one conservative amino acid substitution, the claim encompasses a polypeptide in which none of the amino acids are the same as those of SEQ ID NO:2. There is no function of the polypeptide required by the claim. As stated above, there is no definition of what a DR5 polypeptide is so that one of skill in the art would know what properties the claimed encoding nucleic acid must have in order to encode a DR5 polypeptide. While the specification defines which substitutions are considered conservative (TABLE 1 of page 25) and one would reasonably expect that a limited number of amino acids could be substituted with conservative amino acids, one would not reasonably expect that a substitution of all amino acids of SEQ ID NO:2 or amino acids in a complete domain thereof would yield a protein having the function of the original protein, such as induction of apoptosis (first paragraph of p. 53). Nor could one predict how many amino acids could be conservatively substituted while maintaining activity of the original protein or portion thereof so that one would know how to use a substituted polypeptide. The full-length protein is over 400 amino acids long. Even being limited to conservative amino acid substitutions, there is an enormous number of polypeptides encompassed by the claim. The specification has shown only how to use a polypeptide having the amino acid sequence of SEQ ID NO:2 or specific domain thereof (e.g., extracellular domain, ECD, see Example 6). For these reasons and those above, it would require undue experimentation to make the nucleic acid of

claim 23 wherein the encoded polypeptide had an unlimited number of amino acid substitutions compared to SEQ ID NO:2.

9. Claims 18 and 34 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of producing a polypeptide comprising the sequence of SEQ ID NO:2 or a fragment thereof which is epitope-bearing or which comprises the ECD, ICD, TMD or DD, does not reasonably provide enablement for a method producing a polypeptide which has an amino acid sequence that is not SEQ ID NO:2 or a fragment thereof. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The claims are drawn to a method of producing a polypeptide comprising a fragment of SEQ ID NO:2, or encoded by a nucleic acid which is a complement of a coding sequence (claim 1(j) and 8) or which is 95% identical or hybridizes under stringent conditions to a nucleic acid encoding a polypeptide of SEQ ID NO:2 or fragment thereof. Polypeptides are encoded by the "coding strand" of a nucleic acid, and the complement of the coding strand does not by definition encode. The specification teaches a DR5 polypeptide having the sequence of SEQ ID NO:2. Also taught is an encoding nucleic acid having the sequence of SEQ ID NO:1. It is disclosed that that polypeptide or fragments thereof may be used to produce antibodies and that the extracellular domain and complete polypeptide can influence apoptosis (Examples 5 and 6). However, a nucleic acid which is 95% identical to a nucleic acid which encodes a polypeptide of SEQ ID NO:2 does not necessarily encode anything. According to the specification, such a nucleic acid can include insertions or deletions relative to the reference nucleic acid. This means that nucleic acids with frameshifts are possible so the encoded polypeptide is truncated or a "nonsense" amino acid sequence not related to SEQ ID NO:2. The specification has not taught how to use such polypeptides. Further, because SEQ ID NO:2 can be encoded by a great number of nucleic acids due to degeneracy of the genetic code, the encoding nucleic acid does not need to resemble the naturally occurring encoding nucleic acid of SEQ ID NO:1. This means that a

nucleic acid which is 95% identical to a degenerate nucleic acid would not be useful for isolating related naturally occurring nucleic acids nor would the encoded polypeptide necessarily be structurally similar to the polypeptide of SEQ ID NO:2 since 1/20 amino acids could differ. Further, for the reasons set forth in the previous rejection, the specification is not enabling for a nucleic acid encoding a DR5 domain, and so one could not produce a polypeptide using that nucleic acid. For these reasons, it would require undue experimentation to practice the invention as claimed.

10. Claims 1, 5-9, 14-18, 29-34 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention.

In addition to the enablement issues discussed above in this Office action, elements required for practicing a claimed invention must be known and readily available to the public or obtainable by a repeatable method set forth in the specification. When biological material is required to practice an invention, and if it is not so obtainable or available, the enablement requirements of 35 USC §112, first paragraph, may be satisfied by a deposit of the material. See 37 CFR 1.802.

The specification does not provide a repeatable method for obtaining ATCC Deposit No. 97920, and it does not appear to be a readily available material. For each deposit made pursuant to these regulations, the specification shall contain: (1) The accession number for the deposit; (2) The date of the deposit; (3) A description of the deposited biological material sufficient to specifically identify it and to permit examination; and (4) The name and address of the depository. [See MPEP 2404-2410.02.]

The location and date of deposit of ATCC #97920 is disclosed on p. 7, lines 25-29; however, the deposit does not satisfy the enablement requirements because if a deposit is made under the terms of the Budapest Treaty, then an affidavit or declaration by Applicants or someone associated with the patent owner who is in a position to make such assurances, or a

statement by an attorney of record over his or her signature, stating that the deposit has been made under the terms of the Budapest Treaty and that all restrictions imposed by the depositor on the availability to the public of the deposited material will be irrevocably removed upon the granting of a patent, would satisfy the deposit requirements. See 37 CFR 1.808.

If a deposit is not made under the terms of the Budapest Treaty, then an affidavit or Declaration by Applicants or someone associated with the patent owner who is in a position to make such assurances, or a statement by an attorney of record over his or her signature, stating that the deposit has been made at an acceptable depository and that the following criteria have been met:

(a) during the pendency of the application, access to the deposit will be afforded to one determined by the Commissioner to be entitled thereto;

(b) all restrictions imposed by the depositor on the availability to the public of the deposited material will be irrevocably removed upon the granting of a patent;

(c) the deposit will be maintained for a term of at least thirty (30) years and at least five (5) years after the most recent request for the furnishing of a sample of the deposited material;

(d) a viability statement in accordance with the provisions of 37 CFR 1.807; and

(e) the deposit will be replaced should it become necessary due to inviability, contamination or loss of capability to function in the manner described in the specification. In addition the identifying information set forth in 37 CFR 1.809(d) should be added to the specification. See 37 CFR 1.803-1.809 for additional explanation of these requirements.

Claim Rejections - 35 USC § 112, Second Paragraph

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

11. Claims 1, 8-13, 23 and dependent claims 2-7, 14-18 and 29-34 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1, 8-13 and 23 are indefinite because it is unclear what "the DR5" is including

when specific domains thereof are referred to. It is unclear if it is the mature form (*i.e.*, section (e) of claim 1) or another form. While the specification provides an example of a DR5 (e.g., p. 7, lines 20-22), it is unclear if there are other DR5's, and if there are, how they are related to the one disclosed. Also, it is unclear how a DR5 must differ from other proteins, such as DR3 (Chinnaiyan et al., Science, 1996, cited by Applicants). Therefore, the metes and bounds of the claim are not clear. Note that for claim 10, while approximate fragments of SEQ ID NO:2 are recited, the claim is indefinite because since the sequence of a DR5 is unknown and the range of amino acids is approximately, it is unclear what the epitope-bearing portion is. That is, if the epitope-bearing portion comprises something other than a fragment of SEQ ID NO:2 (which is possible as the claim is written), it is unclear what the metes and bounds of the epitope-bearing portion are.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

12. Claims 8, 9 and 29-31 are rejected under 35 U.S.C. 102(b) as being anticipated by Z66083 (U).

GenBank Accession No. Z66083 teaches a nucleic acid which is 98% identical over nucleotides 80-275 of SEQ ID NO:1 (see "SEQUENCE COMPARIAON—A). The nucleic acid of Accession No. Z66083 is 257 nucleotides long, so that 76% of the nucleic acid of Accession No. Z66083 shares near total identify to the above portion of the SEQ ID NO:1. Therefore, this nucleic acid would hybridize under stringent conditions to the nucleic acid encoding SEQ ID NO:2. The nucleic acid is in pGEM-5ZF vector (in "COMMENTS"). Because of the length of

the Accession No. Z66083 nucleic acid, one would reasonably expect it to encode an epitope-bearing portion of the polypeptide having the sequence of SEQ ID NO:2 of the instant application.

13. Claims 8, 9, 22 and 29-33 are rejected under 35 U.S.C. 102(a) as being anticipated by GenBank Accession No. AA223122 (V).

GenBank Accession No. AA223122 teaches a polypeptide that is 97% identical over nucleotides 236-698 of SEQ ID NO:1 of the instant specification (see attached "SEQUENCE COMPARISON-B"). The nucleic acid of AA223122 is 469 nucleotides long (i.e., the entire length from nucleotides 236-698 of SEQ ID NO:1). Therefor, the nucleic acid would hybridize under stringent condition to a polynucleotide having a nucleotide sequence identical to a nucleotide sequence in any one of (a)-(j) of claim 1. It is also at least 95% identical to at least 50 contiguous nucleotides of SEQ ID NO:1 from 284-1,362 and encodes at least 30 contiguous amino acids of SEQ ID NO:2. The nucleic acid is in the Bluescript SK- vector, which is in the SOLR host cell (see "Source" section). Because of the length of the nucleic acid of AA223122, one would reasonably expect that it would encode an epitope-bearing portion of the polypeptide having the sequence of SEQ ID NO:2 of the instant application.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

> This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later

invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C103(a).

14. Claims 8, 9, 22, 29-34 are rejected under 35 U.S.C. 103(a) as being unpatentable over GenBank Accession No. AA223122 (V) and Chinnaiyan et al. (Science, 1996, cited by Applicants) in view of Sibson et al. (WO 94/01548, N).

GenBank Accession No. AA223122 teaches a polypeptide that is 97% identical over nucleotides 236-698 of SEQ ID NO:1 of the instant specification (see attached "SEQUENCE COMPARISON-B"). The nucleic acid of AA223122 is 469 nucleotides long (i.e., the entire length from nucleotides 236-698 of SEQ ID NO:1). Therefor, the nucleic acid would hybridize under stringent condition to a polynucleotide having a nucleotide sequence identical to a nucleotide sequence in any one of (a)-(j) of claim 1. It is also at least 95% identical to at least 50 contiguous nucleotides of SEQ ID NO:1 from 284-1,362 and encodes at least 30 contiguous amino acids of SEQ ID NO:2. The nucleic acid is in the Bluescript SK- vector, which is in the SOLR host cell (see "Source" section). Because of the length of the nucleic acid of AA223122, one would reasonably expect that it would encode an epitope-bearing portion of the polypeptide having the sequence of SEQ ID NO:2 of the instant application. The nucleic acid is classified as an EST (see "Division Code"). GenBank Accession No. AA223122 does not teach production and recovery of an encoded polypeptide.

Chinnaiyan et al. teach vectors comprising the DR3 receptor-encoding nucleic acid, transfection of mammalian cells, and expression followed by recovery of the receptor by FLAG immunoprecipitation (see legend of Figure 3B).

Sibson et al. teach the desirability of expressing ESTs. It is stated (p. 10, line 38) that "Partial or full length cDNAs have great utility once expressed." And (p. 11, lines 9-10), "The proteins thus-expressed can be screened for activities of therapeutic or commercial value." Also taught is that fragments as short as 8 amino acids in length can be used as antigens for the production of useful antibodies (p. 11, lines 16-22). Also taught is an EST library formed by ligating each DNA piece into a pBluescript vector and transformation of *E. coli* host cell DH5a (p. 19, third paragraph). All methods of expression described by Sibson et al. are old in the art (*e.g.*, p. 8, lines 26-34).

It would have been obvious to express and recover the polypeptide encoded the nucleic acid of GenBank Accession No. AA223122 because Chinnaiyan et al. teach methods of expressing nucleic acids and recovering the products, and Sibson et al. also teach methods as well as the desirability of obtaining such expressed polypeptides, for example for use as antigens.

Conclusion

15. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Claire M. Kaufman, whose telephone number is (703) 305-5791. Dr. Kaufman can generally be reached Monday through Friday from 8:00AM to 4:30PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Paula Hutzell, can be reached at (703) 308-4310.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Official papers filed by fax should be directed to (703) 308-4242. Faxed draft or informal communications with the examiner should be directed to (703) 308-0294. NOTE: If applicant *does* submit a paper by fax, the original signed copy should be retained by the applicant or applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED so as to avoid the processing of duplicate papers in the Office. **Please** advise the examiner at the telephone number above before facsimile transmission.

Claire M. Kaufman, Ph.D.

Patent Examiner, Art Unit 1646

May 21, 1999